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EUROPEAN PATENT APPLICATION

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(54) Utilization of lysolecithins in the treatment of male impotence and alopecia and the relevant compositions suitable for such use.

(57) Compositions based on Lysolecithins are advantageously used in the treatment of male impotence and alopecia and are exempt from adverse side reactions.

EP 0 608 511 A2

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OBJECT OF THE INVENTION

Object of the present invention are the utilization of Lysolecithins in the treatment of male impotence and alopecia and the Lysolecithin-based compositions suitable for such use.

PRIOR ART

Lysolecithins or Lysophosphatidylcholines, which are basic components of the cell membrane, are natural compositions of animal or vegetal origin.

Lysolecithins are obtained by hydrolysis in beta position by Phospholypase A₂ from the corresponding Lecithins of Phosphatidylcholines. Having a good emulsifying power and solubilizing properties, Lysolecithins are utilized mainly in the cosmetic field, as they permit to obtain stable emulsions, to be used for instance for the preparation of creams, milky lotions, ointments, besides being solubilizing agents for after-shave lotions, hair lotions and lotions in general. Besides, they are also utilized for skin and hair care and in soaps. Some "Lysolecithin-like" compositions are also described as being potential carcinostatic agents (Patent JP 8806554) and in general possible applications in the immune-oncologic field are suggested for Lysolecithins and/or compositions obtained from them.

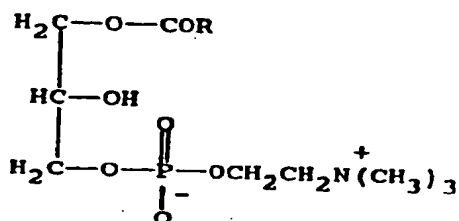
PURPOSES OF THE INVENTION

Purpose of the present invention is to provide a new drug utilizable for the treatment of male impotency.

Another purpose of the present invention is to provide a new drug utilizable for the treatment of alopecia. Still another purpose of this invention is to provide compositions suitable to be utilized for the treatment of male impotence and alopecia and that are exempt from adverse side reactions.

DESCRIPTION OF THE INVENTION

These and still other purposes and related advantages which shall be made clear by the following description are reached by a product constituted by Lysolecithin having the following general formula:



where R are the known characteristic functionalizations of Phosphatidylcholines, and in particular saturated and/or unsaturated fat acids, which product is utilized for the treatment of male impotence and for the treatment of alopecia. In fact, it has been observed that the administration of suitably formulated Lysolecithins causes the dilatation of the cavernous vessels of the penis, facilitating erection, and in the case of alopecia, it activates blood circulation in the scalp, facilitating hair growth. Lysolecithins, according to the present invention, are administered in compositions which comprise, besides excipients and additives of a known type, compounds which are provided with antioxidant characteristics such as, for instance, tocopherol, nordihydroguaiaretic acid, ascorbic acid, butyl-hydroxyanisole and the like, which inhibit the potential chemical degradation characteristic of Lysolecithins, and permit the application of said compositions or formulations, avoiding adverse side reactions, such as local irritations, allergies and the like. According to the present invention, said compositions or formulations are characterized by a content of Lysolecithins comprised between 0.1% and 20%, preferably 0.1 and 10%. Said formulations and compositions containing Lysolecithins, when utilized in the treatment of male impotence or alopecia, are exempt from the adverse side reactions that are characteristic of the utilization of Lysolecithins as such when used in high doses, or in particular experimental conditions, said adverse side reactions being due to cytolytic reactions, and consequently to damages of a cellular type. The drug containing Lysolecithins according to this invention permits therefore to obtain a significant therapeutic activity in the treatment of male impotence and alopecia, allowing the local administration of Lysolecithins in concentrations such as to develop said therapeutic activity without incurring any adverse side reaction. Always according to

the present invention, said compositions or formulations containing Lysolecithin are advantageous utilized as condom lubricants, so as to associate the necessary lubricant activity to the therapeutical activity.

Always according to this invention, said compositions or formulations may comprise many additives and excipients of a known type, in amounts variable according to the characteristics required of the final product, as described in the hereunder illustrated examples, which are given by way of indication with no limitations for the protection scope of this invention.

EXAMPLE 1. Oil/water creamy emulsion

- Soja lysolecithin 5.0 g
- Iso-octilstearate 10.0 g
- Vaseline oil 5.0 g
- Cetyl alcohol 3.0 g
- Polyoxyethylensorbitan monoleate 2.5 g
- Tocopherols 0.5 g
- Carbomer 0.4 g
- Paraseptics 0.2 g
- Distilled water q.s. to 100 g

EXAMPLE 2. Water/oil creamy emulsion

- Soja lysolecithin 7.5 g
- Tocopherols 0.5 g
- Vaseline 10.0 g
- Vaseline oil 10.0 g
- Sorbitan-monolaurate 2.5 g
- Sorbitan-monostearate 2.5 g
- Conservatives 0.2 g
- Distilled water q.s. to 100 g

EXAMPLE 3. Milky solution

- Lysolecithin 1.0 g
- Alpha-tocopherol acetate 0.1 g
- Iso-octilstearate 1.0 g
- Vaseline oil 0.5 g
- Polyoxyethylensorbitan monolaurate 0.2 g
- Paraseptics 0.2 g
- Distilled water q.s. to 100 g

EXAMPLE 4. Solution for the treatment of alopecia

- Lysolecithin 2.5 g
- Tocopherol 2.25 g
- Ethyl alcohol 25.0 g
- Vegetable extracts 0.5 g
- Distilled water q.s. to 100 g

EXAMPLE 5. Solution for the treatment of alopecia

- Lysolecithin 2.5 g
- Tocopherol 0.2 g
- Triethanolamine laurylsulfate 20.0 g
- Alkylamidobetaine 10.0 g
- Lauryl ether sodium sulfate 10.0 g
- Conservatives 0.4 g
- Distilled water q.s. to 100 g

The muscle relaxant activity of the cavernous body in the rabbit has been determined according to the meth-

od described by IGNARRO et al. Biochem. Biophys. Res. Commun. 170,843 (1990).

By way of example, Table 1 shows the per cent activity on the rabbit cavernous body of Lysolecithin suitable vehiculated to make treatment possible; the per cent activity of vehicle only is considered as a reference, treatment conditions being equal. The values shown are a mean of the values obtained from the repetition of 5 tests for each treatment group.

TABLE 1

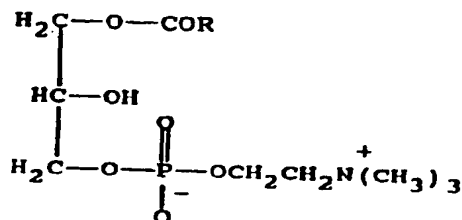
Product	Muscle relaxating % activity on rabbit cavernous body
- Vehiculated Lysolecithin	20
- Vehicle	0

When locally applied on the shaven skin of the guinea pig or in the eye of the rabbit, the product obtained as described in Example 1 and Example 2, according to the present invention, proved to be very well tolerated even if used at concentrations remarkably higher than those that have proved to be efficacious in the specific activity tests.

The efficaciousness and tolerability of the product obtained as described in Example 4 and Example 5, according to the present invention, have been evaluated in patients suffering from alopecia according to the method described by A.C.DE GROOT et al., Lancet 1, 1019 (1987). The treatment has brought to cosmetically acceptable improvements and its tolerability was excellent.

Claims

1. Product constituted by Lysolecithin having the following general formula:



where R are the characteristic functionalizations of phosphatidylcholines, and in particular saturated and/or unsaturated fat acids, characterized in that it is utilized for the treatment of male impotence.

2. Product constituted by Lysolecithin according to claim 1, characterized in that it is utilized for the treatment of alopecia.
3. Compositions containing Lysolecithin according to claims 1 and 2, characterized in that said Lysolecithin is associated with compounds having antioxidant properties, said compositions, utilized in the treatment of male impotence and alopecia, being exempt from adverse side reactions.
4. Compositions according to claim 3, characterized in that said compounds having antioxidant properties are chosen among tocopherol, nordihydroguaiaretic acid, ascorbic acid, butylhydroxyanisole.
5. Compositions containing Lysolecithin according to claims 1 and 2, characterized in that the Lysolecithin content of said compositions is comprised between 0.1 and 20% in weight compared to the total weight of the composition.
6. Compositions containing Lysolecithin according to claims 1 and 2, characterized in that the Lysolecithin content of said compositions is comprised between 1 and 10% in weight compared to the total weight of the composition.

EP 0 608 511 A2

- 7. Compositions containing Lysolecithin according to claim 3, characterized in that they are used as condom lubricants.**

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EUROPEAN SEARCH REPORT

Application Number
EP 93 11 9208

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cls)
X,Y	US-A-4 927 629 (BING) * the whole document *	1-7	A61K31/00 A61K31/685
Y	N.ENGL.J.MED. vol. 320, no. 16, 1989 pages 1025 - 30 * page 1025, left column, line 12 - line 13 * * page 1029, left column, line 12 - line 28 * * page 1030, left column, line 4 - line 15 *	1-7	
X	GENETE RES. vol. 22, no. 2, 1989 pages 193 - 204	1-7	
X	DE-A-41 13 346 (E.LANG) * page 2, line 1 - line 10 * * page 2, line 21 * * page 2, line 60 * * page 3, line 19 - line 20 * * claims 1,5 *	2-7	
X	Darwent Publications Ltd., London, GB; AN 86-242347 & JP-A-61 171 407 (KANEBO) * abstract *	2-7	
X	PATENT ABSTRACTS OF JAPAN vol. 11, no. 163 (C-424)26 May 1987 & JP-A-61 291 514 (KONDO MITSUO) 22 December 1986 * abstract *	2-7	<p>TECHNICAL FIELDS SEARCHED (Int.Cls)</p> <p>A61K</p>
The present search report has been drawn up for all claims			
Place of search THE HAGUE		Date of completion of the search 21 June 1994	Examiner Gerli, P
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons</p> <p>& : member of the same patent family, corresponding document</p>			

EPO FORM (USE ONLY SEARCH)



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CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

- ☐ All claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for all claims.
- ☐ Only part of the claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claims:
- ☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirement of unity of invention and relates to several inventions or groups of inventions, namely:

See sheet -B-

- ☒ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.
- ☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:
- ☐ None of the further search fees has been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:



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EP 93 11 9208 -B-

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirement of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims 1;2-7 (partially): Use of lysolecithins for the preparation of a medicament for the treatment of male impotence; compositions thereof for use in therapy
2. Claims 2-7 (partially): The use as in item 1 for the treatment of alopecia